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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/536,736	03/28/2000	Helge Bastian	C12Q1/68	5490
29425 7590 05/29/2008 LEON R. YANKWICH 201 BROADWAY CAMBRIDGE, MA 02139				
EXAMINER GUZO, DAVID				
ART UNIT		PAPER NUMBER		
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary

Application No.

09/536,736

Applicant(s)

BASTIAN ET AL.

Examiner

David Guzo

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Period for Reply -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 07 February 2008.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 3-17, 22, 24-31, 33-40, 51, 53-57, 59-66, 69-74, 76-81 and 83-100 is/are pending in the application.
- 4a) Of the above claim(s) 6-8, 56, 57, 65 and 66 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-5, 9-17, 22, 24-31, 33-40, 51, 53-55, 59-64, 69-74, 76-81 and 83-94 is/are rejected.
- 7) ☒ Claim(s) 95-100 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-846)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: _____

Detailed Action
Election/Restriction

Claims 6-8 and 56-57 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 1/17/02.

35 USC 102 Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-5, 24, 25, 33, 34, 36, 51, 69, 72, 76-80, 90 and 91 stand rejected under 35 U.S.C. 102(b) as being anticipated by Ogawa et al.

This rejection is maintained for reasons of record in the previous Office Action (mailed 8/8/07) and for reasons outlined below.

Applicants traverse of this rejection hinges upon the argument that unlike the teachings of Ogawa et al., applicants' method involves binding of the nucleic acids to one side of the non-siliceous membrane in the presence of an immobilization buffer. Specifically, applicants on pp. 14-15 of the Remarks, assert:

In contrast to Ogawa's use of ultrafiltration to retain nucleic acid molecules that are larger than the pore size of a particular ultrafiltration membrane, Applicants' process involves charging one side of a non-siliceous membrane and immobilizing the nucleic acids to that side of the non-siliceous membrane by **binding** the nucleic acid molecules

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to the one side of a non-siliceous membrane in the presence of an immobilization buffer. The bound nucleic acid is subsequently eluted (released) and retrieved from the same side on which it was bound. See, e.g., Claim 1 as amended herein. Contaminating proteins and other non-nucleic acid molecules are not so bound to the non-siliceous membrane and therefore can pass through the pores to the other side of the membrane, thereby purifying the nucleic acid that remains bound to the side of the membrane to which the nucleic acids were initially charged. As discussed more fully below, the fact that Applicants' claimed process involves an actual binding of nucleic acids to one side of a non-siliceous membrane and not simply retention on the membrane of nucleic acid molecules that are larger than the membrane's pore size is clearly shown by the fact that excellent yields of purified nucleic acid molecules can be isolated according to Applicants' process even when the non-siliceous membrane has a pore size that is clearly larger than the size of the isolated nucleic acid molecules.

Applicant's arguments filed 2/7/08 have been fully considered but they are not persuasive. In response, the examiner notes that Ogawa et al. recites that the ultrafilter used may be made of any material and Ogawa et al. specifically recites that polysulfone ultrafilters may be employed in the nucleic acid isolation method. Polysulfone is a hydrophobic polymer which inherently **binds nucleic acids** (indeed, applicants in the instant specification recite the desirability of using hydrophobic membranes to bind (immobilize) nucleic acids in the context of the instant invention; see, for example, pages 8-9 of the instant specification). Therefore, the skilled artisan, following the specific teachings of Ogawa et al., would have used a polysulfone ultrafilter in the DNA isolation procedure wherein said ultrafilter would have the inherent property of binding nucleic acids. Applicants' assertion that Ogawa et al. does not teach a nucleic acid isolation procedure involving binding of nucleic acid to the ultrafilter is therefore not persuasive and all other arguments based upon the supposed lack of this teaching in Ogawa et al. are likewise not persuasive.

With regard to applicants' arguments that the process disclosed by Ogawa et al. relies only on mechanical retention of the nucleic acids by the membrane, it is again noted that the use of polysulfone ultrafilters, as specifically recited by Ogawa et al., would result in binding of the nucleic acids to the ultrafilter. Also, applicants' arguments attempting to differentiate the instant invention from the teachings of Ogawa et al. wherein said arguments are based upon a comparison of the instant invention with the specific example recited in Ogawa et al. are not persuasive. The teachings of Ogawa et al. are not limited to the example, but instead are much broader with regard to the pore sizes of the ultrafilters used (fractionation molecular weight of 20,000 to 1,000,000 daltons) to bind/retain the nucleic acids and the composition of said ultrafilters (can be any material and specifically polysulfone).

35 USC 103(a) Rejections

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 9-14, 39, 40, 55, 59-61, 70-72, 77-78, 89 and 92-94 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ogawa et al. in view of Mullis (US 5,234,824). New claims 92-94 are included in the rejection as a result of applicants amendment filed 2/7/08.

Claims 9-17, 22, 26-31, 35, 37-40, 53-55, 59-64, 70, 71, 73-74, 81 and 83-89 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Ogawa et al. in view of Mullis, Pfister et al., Boom et al., Colpan et al. and Macfarlane et al.

The above rejections under 35 USC 103(a) are maintained for reasons of record in the previous Office Action and for reasons outlined below.

With regard to the rejection over Ogawa et al. in view of Mullis, applicants again argue that Ogawa et al. does not teach binding of nucleic acids to the ultrafilter. This argument is incorrect for reasons cited above. Since Ogawa et al. does recite a nucleic acid isolation procedure wherein nucleic acids are bound to the ultrafilter and the immobilization and washing solutions are not restricted, the various salts, detergents and other compounds taught by Mullis in the context of commonly used and well known immobilization buffers and washing solutions would have been obvious embodiments for the ordinary skilled artisan to use in the method of Ogawa et al.

Applicants also assert that Mullis does not teach the limitations of claim 9. Applicants' arguments are not persuasive because the restriction enzyme digestion of

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the nucleic acid trapped in the filter represents an ongoing process wherein the digestion of the nucleic acids starts while the nucleic acids are trapped in the filter and as they are released into solution and present restriction sites which were not available while the molecules were trapped in the filters, continuing restriction digestion occurs and represents digestion after release of the nucleic acids from the filters. Mullis therefore teaches a process whereby the nucleic acids are subject to at least one chemical reaction between release and removal of the nucleic acids for analysis of the digestion.

With regard to the limitations of new claims 92-94, Mullis teaches that filters with pore sizes ranging from 0.2 μm to 0.8 μm (column 5, lines 42-46) can be used in nucleic acid isolation.

With regard to the rejection over Ogawa et al. in view of Mullis, Pfister et al., Boom et al., Colpan et al. and Macfarlane et al., applicants assert that Pfister teaches isolating RNA by binding it to a silica-based fleece, in contrast to the claimed method. In response, the examiner notes that Pfister is not cited for providing a silica based method for isolating RNA, but instead for the solutions used in preparing the nucleic acids compositions for application to the filters.

With regard to the Boom et al. reference, applicants' arguments are essentially those presented in the response filed 6/9/06 and fully addressed by the previous examiner in the Final rejection mailed 8/23/06. The examiner's response is again noted and will not be repeated again here.

With regard to the Colpan et al. and Macfarlane et al. references, applicants analyze said references in isolation and indicate that they do not teach the claimed invention. In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986).

Finally, in response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Miscellaneous

Claims 65-66 (listed as "not entered") are in compliance with 37 CFR 1.121.

Claims 95-100 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of

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the base claim and any intervening claims. The prior art does not teach use of filters with large pore sizes in the claimed ranges to isolate nucleic acids.

No Claims are allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 AM to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach, Ph.D., can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only.

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For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 21, 2008

/David Guzo/
Primary Examiner
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